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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,520	12/21/2001	Jacobus M. Lemmens	ADP-019US	2171

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MARK R. BUSCHER
P.O. BOX 161
CATHARPIN, VA 20143

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,520	LEMMENS ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12,35-37,39-46,49 and 51* is/are pending in the application.

4a) Of the above claim(s) *44-46 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12,35-37,39-43 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 11-29-04 is acknowledged.

Claims included in the prosecution are 1, 3-10, 12, 35-37, 39-43 and 49.

Upon consideration, the 112 and 102 rejections and the double patenting rejection have been withdrawn.

Claim Rejections - 35 USC 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in

section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the

manner in which the invention was made.

2. Claims 1, 3-10, 12, 35-37, 39-43, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable Over Young as set forth in the previous action

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the examiner misread the teachings of Young and that on col. 10, lines 1-5 refer to the crystallization of cinchonidine salt of an azido-acid precursor of amlodipine. According to applicant, the reaction scheme on col. 9 of the reference, the optically pure salt is crystallized to effect the separation of the optical isomers, which are subsequently processed to form pure amlodipine free base. Furthermore, applicant argues that the optically pure amlodipine free base is not taught to be crystallized. These arguments are not found to be persuasive. First of all, instant claims are drawn to two crystalline forms of the free base or a mixture of these forms and applicant has not presented any clear evidence that Young free base forms as seen in example 8 on col. 15 are not crystalline, but only amorphous. Even assuming that Young does not teach the crystallization of the free base, in Example 8, Young teaches the formulations of the free base of amlodipine as tablet formulations and applicant has neither shown that these forms do not leave of instantly claimed residue values or the criticality of the claimed residue values. The examiner also points out that applicant compares the three forms of crystalline forms with amorphous base with a specific combination, that is, in combination with specific amounts of microcrystalline cellulose and calcium sulfate dehydrate. However, the independent claims are generic and recite no ingredients at all (none of the claims recite this specific combination) and there is no evidence to indicate that tablets cannot be prepared using amorphous base in combination with other art known tabletting excipients. Furthermore, according to the results presented in the table, crystalline form II shows a stickiness of 2.93 compared to

the other two forms and appears to leave more residue than that claimed in instant claim 2. Finally, it is interesting to note that on page 5 of the specification, applicant states, "the amlodipine free base can be of any form including crystalline form 1, crystalline form 11, or amorphous." This statement appears to be contradictory to the results in the table, which show that amorphous base cannot form tablets at all.

3. Claims1, 3-10, 12, 35-37, 39-43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5, 155, 120 to Lazar et al in combination with Davison cited and as set forth in the previous action.

Applicant's arguments and the declaration have been fully considered, but are not found to be persuasive. Applicant argues that Lazar generically teaches the use of amlodipine and its salts for treating congestive heart failure and a composition containing amlodipine free base was not made or used in Lazar. This argument is not found to be persuasive since Lazar is suggestive of the use of the free base and applicant has not shown any unexpected results obtained by using the crystalline forms of the base as opposed to presumed amorphous base. With regard to the arguments based on he declaration, the examiner once again points out applicant compares the three forms of crystalline forms with amorphous base with a specific combination, that is, in combination with specific amounts of microcrystalline cellulose and calcium sulfate dehydrate. However, the independent claims are generic and recite no ingredients at all (none of the claims recite this specific combination) and there is no evidence to indicate that tablets cannot be prepared using amorphous base in combination with other art known tabletting excipients. Furthermore, according to the results presented in the

table, crystalline form II shows a stickiness of 2.93 compared to the other two forms and appears to leave more residue than that claimed in instant claim 2. Finally, it is interesting to note that on page 5 of the specification, applicant states, "the amlodipine free base can be of any form including crystalline form 1, crystalline form 11, or amorphous." This statement appears to be contradictory to the results in the table, which show that amorphous base cannot form tablets at all. This rejection is deemed to be applicable since the new claim 43 is drawn to composition containing amlodipine free base and at least one pharmaceutically acceptable excipient.

4. Claims 1, 3-10, 12, 35-37, 39-43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5, 155, 120 to Lazar et al in combination with Young as set forth in the previous action.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments once again are based on the lack of teachings of crystalline compound in the references. The examiner has already addressed these.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GSkishore

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK